IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Tomoharu Suga et al. **ART UNIT**: 1615

SERIAL NO.: 10/542,969 **EXAMINER**: Ahmed, Hasan Syed

FILED: July 21, 2005

FOR: INTRAORALLY RAPIDLY DISINTEGRATING TABLETS AND THEIR PRODUCTION

APPEAL BRIEF IN ACCORDANCE WITH 37 CFR §41.37

MAIL STOP APPEAL BRIEF PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The claimed invention relates to an intraorally rapidly disintegrating tablet which comprises either an active ingredient mixed with at least one sugar or a water soluble active ingredient, either of which constitutes a core, and a pharmaceutically acceptable disintegrating agent substantially completely covering the core to form a granule. The Examiner in a Final Office Action rejected all of the pending claims as anticipated by U.S. Patent No. 5,576,014 to Mizumoto, et al. ("Mizumoto").

Appellants respectfully submit this rejection is in error because Mizumoto clearly teaches that the agent it uses with its core is applied in a coating solution, i.e. in a water solution. It is well known, however, that once a disintegrating agent is exposed to water, it loses its disintegrating properties, even if the agent is subsequently dried. Therefore, it necessarily follows that the Mizumoto coating cannot be a disintegrating agent and accordingly Mizumoto cannot anticipate the claimed invention. In addition, Mizumoto does not teach substantially completely coating the cores. Finally, the Examiner has misconstrued claim 7.

Pursuant to the provisions of 37 CFR §§41.31, 41.35 and 41.37, this brief appeals the

Office Action, marked Final, of Examiner Hasan Syed Ahmed of Art Unit 1615 dated July 7, 2009.

In response to the Final Office Action, and based on the January 7, 2010 filing date of the Notice of Appeal, Appellants submit herewith their Appeal Brief, with reference to the above-identified patent application, together with authorization to charge any requisite deficiency of fees under 37 CFR §1.17 to Deposit Account No. 20-1507, and in conformance with the requirements of 37 CFR §41.37.

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1. REAL PARTY IN INTEREST

The real party in interest in this application is Nippon Shinyaku Co., Ltd., 14, Kisshoin Nishinosho Monguchicho, Minami-ku, Kyoto-shi, Kyoto 601-8550 Japan. The assignment for this application was recorded on July 21, 2005 at Reel 017514, Frame 0974.

2. RELATED APPEALS AND INTERFERENCES

No other appeals or interferences in connection with the present application are known to Appellants, Appellants' legal representative, or assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

3. STATUS OF CLAIMS

Claim 1 has been cancelled. Claims 2-10 are pending. All pending claims stand finally rejected. Claims 2-10 are on appeal.

4. STATUS OF AMENDMENTS

No amendments have been filed subsequent to the Final Office Action dated July 7, 2009 (hereinafter the "Final Office Action"). All prior amendments have been entered and considered by the Examiner.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is directed toward an intraorally rapidly disintegrating tablet. The tablet includes a core which is either an active ingredient mixed with at least one sugar or a water soluble active ingredient. The core is substantially completely covered by a coating of a pharmaceutically acceptable disintegrating agent.

There are two independent claims, claims 6 and 7. Both claims relate to an intraorally rapidly disintegrating tablet. See Specification at the Abstract; page 1, lines 4-5; page 3, lines 2-3 and 11-12; and original claims 1-5. Claim 6 claims a tablet which first comprises an active ingredient mixed with at least one sugar to form a core. See Specification at the Abstract; page 3, line 16; page 10, line 21; page 14, line 15; Examples 1-12 at pages 16-23; and original claim 1. The tablet of claim 6 further comprises a pharmaceutically acceptable disintegrating agent substantially completely covering said core to form a granule. See Specification at the Abstract; page 3, lines 7-8 and 13; page 4, lines 4-6; page 11, lines 8-11; page 14, line 9 – page 15, line 5;

Examples 1-12 at pages 16-23; and original claim 1.

Claim 7 is similar in scope to claim 6, except the tablet of claim 7 comprises a water soluble active ingredient which constitutes a core. See Specification at the Abstract; page 3, line 15; page 14, line 14 and original claim 1.

Claims 2 and 8 depend from claims 6 and 7, respectively, and claim specific types of pharmaceutically acceptable disintegrating agents which can be used. See Specification at page 4, lines 7-15 and original claim 2. Claim 3 is dependent from claim 6 and claims specific types of sugars which can be used. See Specification at page 3, line 18 – page 4, line 2 and original claim 3. Claims 4 and 9 are dependent from claims 6 and 7, respectively, and claim tablets where the average particle diameter of the granules is in the range of 20 to 1000 μm. See Specification at page 4, line 20 and original claim 4. Finally, claims 5 and 10 are dependent from claims 6 and 7, respectively, and claim tablets whose thickness is in the range of 1 to 10 mm. See Specification at page 14, line 3 and original claim 5.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether claims 2-10 are invalid under 35 U.S.C. §102(b) as being anticipated by Mizumoto.

7. ARGUMENT

A. Introduction

The fundamental flaws in the Examiner's rejection are his belief that Mizumoto teaches coating cores with a disintegrating agent and his belief that Mizumoto teaches substantially completely coating the cores. These flaws were discussed in detail in the Declaration of Hiroshi Fukui dated May 15, 2007. In addition, the Examiner has misconstrued claim 7. In claim 7, the core is water soluble active ingredient, not an active ingredient mixed with at least one sugar.

B. The Examiner's Rejection

At page 2 of the Final Office Action, the Examiner contended Mizumoto at column 7, lines 19-46 and column 13, lines 39-43 teaches coating a core granule with the pharmaceutical disintegrating agent of claims 6 and 7. He also contended Mizumoto at column 13, lines 5-7, 36-41 and 58-63 teaches the substantially complete covering of claims 6 and 7, i.e. a high moldability saccharide coating mixed with disintegrating agents. He further contended

Mizumoto at column 12, lines 24-26 teaches an active ingredient mixed with a sugar. At pages 3 and 4 of the Final Office Action, the Examiner contended that in the present invention, when the disintegrating agent is added, 1/3 of the binder solution still remains and therefore the disintegrating agent is being directly added to water. Accordingly, per the Examiner, the coating of Mizumoto reads on the instantly claimed invention.

For reasons set forth below, Appellants respectfully submit that the Examiner's analysis is in error.

C. Mizumoto Does Not Teach The Use Of A Disintegrating Agent

Paragraphs 6-12 of the Fukui Declaration describe why Mizumoto does not disclose the use of a disintegrating agent as claimed.

Starting in column 13, line 32, Mizumoto identifies various optional additives which can be added to its tablets, including disintegrating agents. See column 13, lines 39-43. In column 13, lines 58-65, Mizumoto describes how these optional ingredients are added.

> These additive agents may be used alone or as a mixture of two or more in an appropriate amount at an optional step in the production process of the intrabuccally dissolving compressed moldings, for example, when an active ingredient is mixed with a low moldability saccharide, when a coating solution prepared by dissolving an active ingredient together with a high moldability saccharide in water is mixed, or at a step before or after these steps.

This means that in Mizumoto the disintegrating agent may be added to a coating solution. Fukui Declaration paragraph 10. This makes no sense, however, because once a disintegrating agent fully absorbs water, it can no longer function as a disintegrating agent. This is true even if the disintegrating agent is subsequently dried. Fukui Declaration paragraphs 10-11. Since in Mizumoto the "disintegrating agent" is added to a coating solution and thus fully absorbs water, it loses its disintegration properties. That is, it is no longer a disintegrating agent.

In contrast, in the invention on appeal, the disintegrant is basically coated onto the core granule in a solid state, i.e. a powder. Fukui Declaration paragraph 12. This is different from the procedure followed in Mizumoto. Since the disintegrant is added as a powder, i.e. dry, it retains is disintegrating properties.

In his Response to Arguments starting at page 3 of the Final Office Action, the Examiner does not dispute Appellants' representations as to Mizumoto. Rather, the Examiner believes that in the instantly claimed invention, "the disintegrating agent is being directly added to water" because in, for example, Example 1, when the disintegrating agent is added, 1/3 of the binder solution remains. Therefore, per the Examiner, the coating of Mizumoto reads on the claimed invention. Appellants respectfully submit that the Examiner is misreading the instantly claimed invention.

Example 1 is set forth at pages 16-17 of specification. As noted therein, the disintegrating agent (corn starch) was gradually added to the cores only after the volume of binding solution was reduced to 1/3. While it is true that some moisture might still be present, this is explained in paragraph 12 of the Fukui Declaration which notes that "the surface of the disintegrant comes in contact with water for a moment". This momentary contact with water, however, is not sufficient to destroy the disintegrating properties of the disintegrant.

That the disintegrant of the instant invention still functions as a disintegrant is clear from Table 1 at page 25 of the specification. As shown, Example 1 has a disintegration time of 40-45 seconds in the oral cavity. Reference is also made to Example 5. As shown at page 19 of the specification, in Example 5 the disintegrating agent was also added after the volume of the binder solution was reduced to 1/3. As shown in Table 1, Example 5 has a disintegration time of 30-35 seconds in the oral cavity.

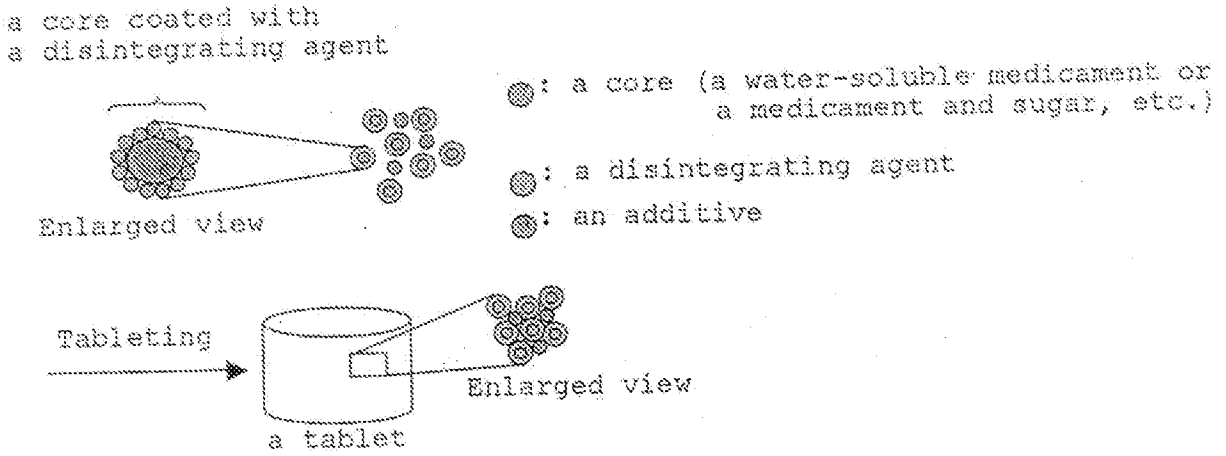
The above data demonstrate that the momentary contact with water in the instant invention is not sufficient to destroy the disintegrating properties of the disintegrating agent. Therefore, and contrary to the Examiner's statement at page 4 of the Final Office Action, the coating of Mizumoto does not read on the instant invention because the coating of Mizumoto does not function as a disintegrating agent. See Fukui Declaration at paragraphs 11 and 12. In contrast, the coating of the instant invention does function as a disintegrating agent. See Table 1 at page 25 of the specification.

For these reasons, Mizumoto does not anticipate claims 2-10.

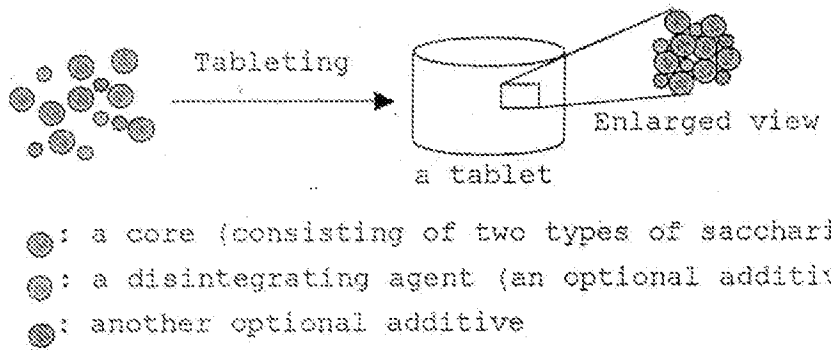
D. Mizumoto Does Not Teach Substantially Completely Coating The Cores With Disintegrating Agent

As set forth in paragraphs 4-7 of the Fukui Declaration, the instantly claimed invention

claims an intraorally disintegrating tablet where the cores themselves are coated with a pharmaceutical disintegrating agent. The structure of the claimed tablet can be visualized as follows:



In contrast, Mizumoto does not disclose a tablet where the cores themselves are coated with a pharmaceutical disintegrating agent. Rather, Mizumoto teaches that the "disintegrating agent" may be generally used in the course of production of tablets (*see* col. 13, lines 32-38) if necessary. The structure of the Mizumoto tablets can be visualized as follows:



Thus, in Mizumoto the "disintegrating agent", if used, is simply mixed with the other ingredients. There is no coating of cores.

Mizumoto attains adequate hardness and quick disintegration by tabletting core granules comprising a saccharine having low moldability and a saccharine having high moldability. See Mizumoto at col. 6, lines 4-16 and col. 7, lines 3-46. In Mizumoto, "disintegrating agents" may be simply used as optional additives. See Mizumoto at col. 13, lines 32-38 and col. 20, claim 16.

In comparison, the presently claimed invention attains an adequate hardness and quick disintegration by tabletting core granules which are coated with a disintegrating agent. Thus, in the present invention, disintegrating agents are required indispensably.

The above arguments are another reason why Mizumoto does not anticipate the claimed invention.

E. The Examiner Has Misconstrued Claim 7

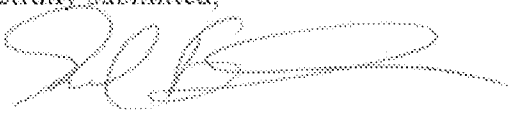
At page 2 of the Final Office Action, the Examiner cites column 12, lines 24-26 of Mizumoto as disclosing the active ingredient mixed with a sugar of claim 6 of the application. Claim 7, however, is different. Claim 7 relates to a water soluble active ingredient, without the mention of a sugar. The Examiner has failed to show where Mizumoto discloses such a core. Appellants believe the Examiner may have misconstrued claim 7, believing its core is the same as that in claim 6. It is not, and since the Examiner has failed to cite where Mizumoto discloses the core of claim 7, Mizumoto cannot be read to anticipate claim 7 (or claims 8-10) which depend from it.

CONCLUSION

In view of the foregoing, it is respectfully submitted that pending Claims 2-10 are patentable over Mizumoto. Reversal of the final rejection under 35 U.S.C. §102, and issuance of a *Notice of Allowance* for pending Claims 2-10, are thus respectfully requested.

Dated: April 16, 2010

Respectfully submitted,



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8. CLAIMS APPENDIX

The following Claims (Claims 2-10) are the only pending Claims, and have been finally rejected and are on appeal.

2. The intraorally rapidly disintegrating tablet according to claim 6, wherein the pharmaceutically acceptable disintegrating agent is a compound selected from the group consisting of crystalline cellulose, low-substituted hydroxypropyl cellulose, carboxymethyl cellulose, calcium carboxymethyl cellulose, crospovidone and starch represented by potato starch, wheat starch, corn starch, rice starch, hydroxypropyl starch, sodium carboxymethyl starch, and partial-pregelatinized starch.

3. The intraorally rapidly disintegrating tablet according to claim 6, wherein the sugar is selected from the group consisting of sugar alcohol represented by mannitol, xylitol, sorbitol, erythritol, maltitol and maltose; lactose, sucrose, glucose, and oligosaccharide.

4. The intraorally rapidly disintegrating tablet according to claim 6, wherein the average particle diameter of the granules is in the range of 20 to 1000μm.

5. The intraorally rapidly disintegrating tablet according to claim 6, wherein the thickness of the tablet is in the range of 1 to 10mm.

6. An intraorally rapidly disintegrating tablet which comprises:

an active ingredient mixed with at least one sugar to form a core and a coating of a pharmaceutically acceptable disintegrating agent substantially completely covering said core to form a granule.

7. An intraorally rapidly disintegrating tablet which comprises:

a water soluble active ingredient which constitutes a core and a coating of a pharmaceutically acceptable disintegrating agent substantially completely covering said core to form a granule.

8. The intraorally rapidly disintegrating tablet according to claim 7, wherein the pharmaceutically acceptable disintegrating agent is a compound selected from the group consisting of crystalline cellulose, low-substituted hydroxypropyl cellulose, carboxymethyl

cellulose, calcium carboxymethyl cellulose, crospovidone and starch represented by potato starch, wheat starch, corn starch, rice starch, hydroxypropyl starch, sodium carboxymethyl starch, and partial-pregelatinized starch.

9. The intraorally rapidly disintegrating tablet according to claim 7, wherein the average particle diameter of the granules is in the range of 20 to 1000μm.

10. The intraorally rapidly disintegrating tablet according to claim 7 wherein the thickness of the tablet is in the range of 1 to 10mm.

9. EVIDENCE APPENDIX

None.

10. RELATED PROCEEDINGS APPENDIX

None.